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**REMARKS**

Claims 46, 49-62, 65, 89 and 90 are pending and under examination in the subject application. Applicants have not added, canceled or amended any claim. Accordingly, claims 46, 49-62, 65, 89 and 90 are still pending and under examination.

**Rejection under 35 U.S.C. §112, First Paragraph**

In the June 26, 2006 Office Action, the Examiner rejected claims 46, 49-62, 65, 89 and 90 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Applicants understand the Examiner's rationale in support of his rejection to be as follows:

1. 35 U.S.C. §112, first paragraph states that the "specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."
2. The Examiner interprets the term "subject" in claim 46 as encompassing both the organ recipient and the organ donor.

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3. The Examiner notes that the only experimental example of protectively treating a subject from an ischemic disorder as a result of organ transplantation described in the specification involved the administration of carbon monoxide to an organ donor, referring to Example 11 in the specification.
4. The Examiner further notes that there is no explicit disclosure in the specification of treating an organ recipient.
5. Based on point 4, the Examiner states that the claims, which read on treating both the organ donor and the organ recipient, fail to "reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention (See page 2 of the Office Action and the lower right box in the table on page 3 of the Office Action).
6. Based on points 1-5, the Examiner concludes that the application fails to provide an adequate written description for the claims, interpreted as in point 2.

In response, applicants do not disagree with the Examiner's points 1-4. In fact, applicants' expert, Irving L. Kron, M.D., generally agrees with the Examiner's points 2-4 (See paragraphs 6- 8 of Dr. Kron's declaration, attached hereto as **Exhibit 1**).

However, applicants disagree with the Examiner's points 5 and 6 and maintain that for the reasons that follow, the application reasonably conveys to one skilled in the art that applicants have

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invented the subject matter which is claimed, i.e., a method applicable to treating a "subject", where the "subject" can be either the donor or the recipient of a transplanted organ.

With respect to the Examiner's point 4, applicants note the written description requirement is satisfied if the knowledge and level of skill in the art would permit one skilled in the art to immediately envisage the product claimed (see M.P.E.P. §2163(I)(A) citing *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996)). An explicit description of the claimed invention is not needed to satisfy the written description requirement. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, adequate written description is met (see M.P.E.P. §2163(II)(A)(3)(a) citing *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972)).

With respect to the Examiner's point 5, applicants note that the inquiry whether the application reasonably conveys to a person skilled in the art that the inventors were in possession of the claimed invention is primarily factual and depends on the nature of the invention and the level of knowledge imparted to those skilled in the art by the disclosure at the time the application was filed (see M.P.E.P. §2163(II)(A) citing *In re Wertheim*, 541 F.2d at 262, 191 USPQ at 96). Here, the relevant art is the field of organ transplantation, and one skilled in the art would be someone with experience in the field of organ transplant surgery, both in performing procedures and in research.

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Applicants further note that that (a) there is a strong presumption that an adequate written description of an invention is present when the claimed invention is described in the application as filed (see M.P.E.P. §2163(II)(A) citing *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)), and (b) rejection of a claim for lack of written description should be rare (see M.P.E.P. §2163(II)(A)).

Applicants' position is that the application does reasonably convey to persons skilled in the art that applicants had invented the subject matter of the currently pending claims. Applicants maintain that one skilled in the art would understand that the claimed method encompasses and is applicable to both treating an organ recipient and treating an organ donor, and note the following:

1. The Examiner himself understands the term "subject" to refer to both the organ donor and the organ recipient. Thus, the Examiner states on page 3 of the Office Action that "with respect to organ transplantation..., there are two subjects, the organ donor and organ recipient" and further on page 3, that applicants are "clearly claiming treating the organ donor as well as the organ recipient..."
2. One skilled in the art would not understand the term "subject" to be limited to the donor of a transplanted organ because the term "donor" is used only in example 11 of the specification, beginning on page 133, line 34. In all other instances discussing organ transplant surgery, the term "subject" is used (For example, see page 19, line 36 and page 21, line 12

of the specification). The terms "donor" and "subject" are not used interchangeably. Therefore, the terms "donor" and "subject" have different meanings, and "donor" is an explicitly disclosed subcase of "subject", while "recipient" is a subcase of "subject" that was not explicitly disclosed but is well known in the art. (See also paragraphs 9 and 10 of the declaration of Dr. Kron.)

3. As of the September 27, 1996 effective filing date of the application, it was well known that ischemic injury occurred in both the organ donor and the organ recipient during organ transplantation. (See also paragraphs 11-15 of the declaration of Dr. Kron.)
4. As of September 27, 1996, persons skilled in the art regularly used the term "subject" in the context of organ transplant surgery to refer to the organ recipient. (See also paragraph 16 of the declaration of Dr. Kron and the abstracts cited therein and attached thereto.) Applicants have also submitted complete copies of the articles which correspond to these abstracts as part of the Supplemental Information Disclosure Statement included herein.
5. One skilled in the art, in the context of this application, would understand that the term "subject" refers to both the organ recipient and the organ donor and the method claimed is applicable to both. (See also paragraph 17 of the declaration of Dr. Kron.)

For the preceding reasons, applicants maintain that as of September

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27, 2006, the application clearly described the claimed invention so that one skilled in the relevant art would have understood applicants were in possession of the claimed method, i.e., a method for protectively treating a subject from an ischemic disorder as a result of organ transplantation, wherein the subject be either an organ recipient or an organ donor. Accordingly, applicants request that the Examiner reconsider and withdraw the ground for rejection under 35 U.S.C. §112, first paragraph, for the alleged lack of adequate written description.

#### **Supplemental Information Disclosure Statement**

This Information Disclosure Statement is submitted to supplement the Information Disclosure Statements filed October 3, 2003; June 15, 2004; September 16, 2004; December 30, 2004; April 10, 2006 and August 11, 2006. In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are also listed on the attached Form PTO-1449 attached hereto as **Exhibit 2**.

1. McCord, J.M. "Oxygen-Derived Free Radicals in Post-Ischemic Tissue Injury", N. Engl. J. Med. 1985 Jan. 17; 312(3): 159-63, a copy of which is attached as **Exhibit D** to Dr. Kron's Declaration;
2. Unruh, H.W. "Lung Preservation and Lung Injury" Chest Surg. Clin. N. Am. 1995 Feb.; 5(1): 91-106, a copy of which is attached as **Exhibit E** to Dr. Kron's Declaration;
3. Novick, R.J., et al. "New Trends in Lung Preservation: A

- Collective Review", J. Heart Lung Transplant. 1992 Mar-Apr; 11 (2 Pt 1): 377-92, a copy of which is attached as **Exhibit F** to Dr. Kron's Declaration;
4. Johnson, C.P., et al. "Factors influencing weight gain after renal transplantation", abstract, Transplantation. 1993 Oct.; 56(4): 822-7, a copy of which is attached as **Exhibit G** to Dr. Kron's Declaration;
  5. Murphy, B.G., et al. "Effect of immunosuppressive drug regime on cardiovascular risk profile following kidney transplantation", abstract, Atherosclerosis. 1995 Aug.; 116(2): 241-5, a copy of which is attached as **Exhibit H** to Dr. Kron's Declaration;
  6. Weston, M.W., et al. "Normalization of circulating atrial natriuretic peptides in cardiac transplant recipients", abstract, Am. Heart J. 1994 Jan.; 127(1): 129-42, a copy of which is attached as **Exhibit I** to Dr. Kron's Declaration;
  7. Lambert, S.B., et al. "Bronchoalveolar lavage fluid endotoxin elevation in human single lung transplant recipients during rejection", abstract, Transpl. Immunol. 1995 Mar.; 3(1):81-5, a copy of which is attached as **Exhibit J** to Dr. Kron's Declaration;
  8. Keefe, E.B. et al., "Controversies in patient selection for liver transplantation", abstract, West. J. Med. 1993 Nov.; 159(5):586-93, a copy of which is attached as **Exhibit K** to Dr. Kron's Declaration.

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9. Ryter, S.W., et al. "Therapeutic applications of carbon monoxide in lung disease", Current Opinion in Pharmacology. 2006, 6:257-262, a copy of which is attached as **Exhibit 3**;
10. Mayr, F.B., et al. "Effects of Carbon Monoxide Inhalation during Experimental Endotoxemia in Humans", Am. J. Respir. Crit. Care Med. 2005, Vol. 171: 354-360, a copy of which is attached as **Exhibit 4**;
11. Dolinay, T., et al. "Can Inhalation Carbon Monoxide Be Utilized As A Therapeutic Modality In Human Diseases?", Breath Analysis for Clinical Diagnosis and Therapeutic Monitoring, ed. Amann, A. and Smith D. May 2005: 203-237, a copy of which is attached as **Exhibit 5**;
12. Johnson, C.P., et l. "Factors influencing weight gain after renal transplantation", Transplantation. 1993 Oct.; 56(4): 822-7, a copy of which is attached as **Exhibit 6**;
13. Murphy, B.G., et al. "Effect of immunosuppressive drug regime on cardiovascular risk profile following kidney transplantation", Atherosclerosis. 1995 Aug.; 116(2): 241-5, a copy of which is attached as **Exhibit 7**;
14. Weston, M.W., et al. "Normalization of circulating atrial natriuretic peptides in cardiac transplant recipients", Am. Heart J. 1994 Jan.; 127(1): 129-42, a copy of which is attached as **Exhibit 8**;



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15. Lambert, S.B., et al. "Bronchoalveolar lavage fluid endotoxin elevation in human single lung transplant recipients during rejection", Transpl. Immunol. 1995 Mar.; 3(1):81-5, a copy of which is attached as **Exhibit 9**; and
16. Keeffe, E.B. et al., "Controversies in patient selection for liver transplantation", West. J. Med. 1993 Nov.; 159(5):586-93, a copy of which is attached as **Exhibit 10**.

Applicants request that the Examiner consider these references, initial the attached Form PTO-1449 and make the references of record in the subject application.

#### **Summary**

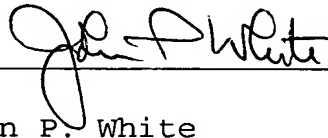
For the reasons set forth hereinabove, applicants respectfully request that all the claims of this application be allowed, and that the application proceed to issuance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee, other than the \$1020.00 fee for a three-month extension of time and the \$180.00 fee for filing a Supplemental Information Disclosure Statement under 37 C.F.R. §1.17(p), is deemed necessary in connection with the filing of this Communication. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

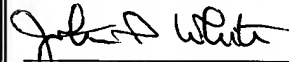
Respectfully submitted,



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